



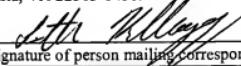
PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Saint-Remy et al.	Confirmation No.:	9175
Serial No.:	10/556,851	Art Unit:	1644
371(c) Date:	February 1, 2006	Examiner:	Michael E. Szperka
Customer No.:	21559		
Title:	VARIABLE ANTIBODIES		

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY TO RESTRICTION REQUIREMENT

In reply to the Restriction Requirement that was mailed in connection with the above-captioned case on January 25, 2008, Applicants elect the invention of Group I, claims 34-45 and 47. The election is made with traverse.

The Office states that the inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2, they lack a special technical feature over Jacquemin et al. (WO 01/04269; hereafter "Jacquemin") in view of Co et al. (U.S. Patent No. 5,714,350; hereafter "Co"). The Office states that Jacquemin discloses "the KRIX-1 antibody that binds FVIII;" Co discloses that "therapeutic antibodies are to comprise modified glycosylation to improve therapeutic

efficiency;" and that "it would have been obvious to a person of ordinary skill in the art at the time of the invention to modify the glycosylation of the KRIX-1 antibody to gain the advantages disclosed by Co et al." (Office Action, page 2). Applicants respectfully disagree and submit that the combination of Jacquemin and Co do not teach or suggest the invention of the claims 34-57.

Co teaches modification of the glycosylation pattern of the variable region of an antibody in order to alter (increase) the affinity of the immunoglobulin for its corresponding antigen (*see*, for e.g., the title of the application, "Increasing Antibody Affinity by Altering Glycosylation in the Immunoglobulin Variable Region"). The method of Co is of interest for increasing the therapeutic potential of the antibody. Accordingly, application of Co to the antibodies described in Jacquemin, would result in antibodies having increased affinity.

The present invention, however, relates to antibodies with modified glycosylation in the variable domain in which the binding affinity of the unmodified antibody is *maintained*. This is apparent from the specification, which describes the definition of a modified antibody according to the invention as follows (page 16, lines 1-4): A "modified antibody" or "modified antibody fragment" as used herein refers to an antibody, which in comparison to the wild-type antibody, is different with respect to its size, more particularly, which is different either with respect to its glycosylation[,] but with a *similar affinity* to its ligand as the wild-type antibody." (Emphasis added.) Moreover, the feature of maintaining affinity is recited in claim 34:

34. An antibody or fragment thereof which is a modified antibody or modified fragment of an inhibitory antibody against FVIII, characterized in that the glycosylation of its variable region has been modified and in that it has substantially the same affinity to FVIII compared to the native antibody. (Emphasis added.)

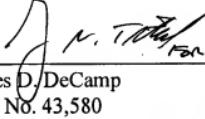
The aim of the modification of the antibodies according to the claimed invention is to ensure a reduced inhibition of factor VIII activity, while maintaining substantially the same affinity for factor VIII compared to the native antibody.

Co, alone or in combination with Jacquemin, fails to teach or suggest that modification of the glycosylation of an antibody can result in reduced inhibition of the activity of the target protein (against which the antibody is directed), while maintaining substantially the same affinity of the antibody for the target. Co, in fact, teaches away from the present invention by suggesting glycosylation necessarily affects binding affinity. Accordingly, as Co and Jacquemin, alone or in combination, fail to disclose or suggest the single general concept encompassed by the pending claims, the restriction requirement should therefore be withdrawn.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 27 February 2008



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